REMARKS

Claims 1-4 and 8-13 are pending. Applicant has amended claim 1 to recite "wherein the maximum concentration of the active ingredient in plasma is about 150 ng/ml or less, and wherein the ratio of the maximum concentration to the minimum concentration of the active ingredient in plasma is about 91 or less." The specification supports this claim amendment at, for example, page 23, lines 7-13 and page 26, line 25 to page 27, line 23. Thus, no new matter has been added.

Regarding Applicant's claim to priority to Japanese patent application 2004-292611, the Examiner has still not indicated whether this claim to priority has been acknowledged. Accordingly, Applicant earnestly requests clarification of the status of the claim to priority.

Applicant acknowledges with appreciation the Examiner's withdrawal of the rejection of claims 1-4 and 7 under 35 U.S.C. § 102(b) as allegedly anticipated by Suzuki et al. (*J. Pharmacol. Exp. Ther.* 275:728-36 (1995); "*Suzuki*") and the rejection of claims 1, 2, and 7 under 35 U.S.C. § 102(b) as allegedly anticipated by Shin-Ichi et al. (WO 92/20683; "*Shin*"). The Examiner rejects claims 1-4 and 8-13 under one or more of 35 U.S.C. §§ 112, second paragraph, 102(b) and 103(a). Applicant addresses these rejections below.

Rejection Under 35 U.S.C. § 112

The Examiner rejects claims 1-4 and 8-13 under 35 U.S.C. § 112, second paragraph, as allegedly indefinite for reciting the phrase "a sustained release composition." (Office Action at page 2.) According to the Examiner, this phrase is understood in the art to mean drug release that occurs over a long period of time. (*Id.*) Noting that the claims also recite a release profile of 2-24 hours or 3-24 hours, the

Examiner apparently does not understand how the claimed composition can be a sustained release composition and still release the drug (Compound A) in 2 to 3 hours. (*Id.*) Applicant respectfully disagrees.

In making this rejection, the Examiner improperly imposes his own understanding of the phrase "a sustained release composition" over the specification's instruction on this term. Indeed, the M.P.E.P. provides at § 2173.01:

> A fundamental principle contained in 35 U.S.C. 112, second paragraph is that applicants are their own lexicographers. They can define in the claims what they regard as their invention essentially in whatever terms they choose so long as any special meaning assigned to a term is clearly set forth in the specification. . . . As noted by the court in *In re Swinehart*, 439 F.2d 210, 160 USPQ 226 (CCPA 1971), a claim may not be rejected solely because of the type of language used to define the subject matter for which patent protection is sought.

Regardless of what the Examiner believes the phrase "a sustained release composition" means in the art, the specification clearly defines this phrase consistently with its usage in the rejected claims. For example, at page 19, lines 16-23, the specification explains that the term "sustained release" means "slow administration of the compound A or its gradual release from a pharmaceutical composition." In turn, the phrases "slowly administer" and "gradually release" mean that "a drug contained in a pharmaceutical preparation is administered or released, for example, during a period of from 2 hours to 24 hours, preferably from 3 hours to 24 hours, more preferably from 5 to 24 hours." Thus, the specification considers a drug release period of 2 hours or 3 hours to be within the release period for a sustained release composition. Accordingly, claims 1-4 and 8-13 are definite in light of the specification's teachings. Applicant therefore requests that this rejection be withdrawn.

Rejection Under 35 U.S.C. § 102(b)

Claims 1, 3-4, and 8-12 stand rejected under 35 U.S.C. § 102(b) as allegedly anticipated by Brann et al. (U.S. Patent 6,528,529; "*Brann*"). (Office Action at page 3.) *Brann* allegedly teaches compounds with activity on muscarinic receptors, including compounds that are the same as those recited in the instant application and teaches sustained release preparations. (*Id.*) *Brann* also allegedly teaches several dosage forms including tablets, pills, capsules, powders, granules, elixirs, tinctures, syrups, emulsions, sterile parenteral solutions, aerosols, drops, and ampoules. (*Id.*) The Examiner contends that all of the dosage forms usually include carriers. (*Id.*) According to the Examiner, *Brann* also teaches the use of PEG and polyvinyl pyrrolidone. (*Id.*) Based on the reasoning that the same compounds have the same properties, the Examiner "assumes" that the release profile recited in claims 1 and 8-10 would be the same. (*Id.*) Applicant traverses.

As the specification explains, several parameters can affect the release rate of a sustained release preparation. For example, the release rate can be adjusted by changing the blending ratio of the hydrophilic base and the hydrogel-forming high molecular weight substance; by adjusting the amount of semipermeable membrane used to coat the composition, adjusting the amount of osmopolymer in the push layer of the composition, and adjusting the molecular weight of the hydrophilic polymer in the sustained release composition. See page 32, lines 11-17; page 36, lines 16-20; page 40, lines 11-14. In addition to modulating the chemical composition of the sustained release formulation, one can also adjust the physical structure of the formulation by having introducing layers into the formulation, each layer having a different role in

delivery of the drug to the recipient. See page 39, line 16 to page 40, line 14. These layers can be changed to thicknesses and shapes to further modulate release rates. See page 41, line 24 to page 42, line 8. Given the factors that can affect the release rate of a drug from a sustained release formulation, *Brann*'s isolated teaching of PEG and polyvinyl pyrrolidone falls very short of constituting a teaching of a sustained release formulation with the specific drug release rate recited in claim 1. Just because these chemicals may be contemplated for use in *Brann*'s compositions does not mean that they will automatically result in the claimed release rates. Thus, the Examiner's assumption is incorrect.

Solely to facilitate prosecution and without acquiescing in the rejection, however, Applicant amended claim 1 to recite "a sustained release composition . . . wherein the release rate of the active ingredient from the composition is from about 4 percent per hour to about 50 percent per hour, wherein the maximum concentration of the active ingredient in plasma is about 150 ng/ml or less, and wherein the ratio of the maximum concentration to the minimum concentration of the active ingredient in plasma is about 91 or less." *Brann* does not teach a sustained release composition in which the "maximum concentration of the active ingredient in plasma is about 150 ng/ml or less." Nor does Brann teach a sustained release composition in which the "ratio of the maximum concentration to the minimum concentration of the active ingredient in plasma is about 91 or less."

Because *Brann* fails to teach all the elements of independent claim 1, this reference cannot anticipate claim 1 or dependent claims 3-4, and 8-12. Applicant therefore requests that the Examiner withdraw this rejection.

Rejection Under 35 U.S.C. § 103(a)

The Examiner rejects claims 1-10 under 35 U.S.C. § 103(a) as allegedly obvious over *Brann* in view of *Suzuki* or *Shin* and in further view of U.S. Patent 6,699,503 ("*Sako*"). (Office Action at page 4.) Because claims 5-7 are canceled, Applicant assumes that the Examiner intended to apply this rejection to claims 1-4 and 8-10. If Applicant's assumption is incorrect, Applicant requests clarification from the Examiner on which claims are addressed by this rejection.

In this rejection, the Examiner applies *Brann* as discussed above and acknowledges that *Brann* does not disclose the tartrate salt of the claimed compound. (*Id.*) *Suzuki* and *Shin* allegedly disclose the use of the L-tartrate form as recited in claim 2. (*Id.* at page 5.) Based on these alleged teachings, the Examiner concludes that it would have been obvious to produce 2,8-dimethyl-3-methylele-1-oxa-8-azaspiro[4.5]decane in a sustained-release form to prolong the action of the compound on lacrimal and salivary glands and produce it tartrate salt because this form allegedly has a superior storage stability. (*Id.* at pages 5 and 6.) The Examiner also acknowledges that none of *Brann*, *Suzuki*, or *Shin* teaches the use of polyethylene oxide as a polymer for a sustained release formulation. Turning to *Sako*, the Examiner contends that this reference teaches a hydrogel-type sustained-release preparation capable of releasing a drug in which one of the hydrogel polymers is polyethylene oxide (PEO). (*Id.* at page 6.) *Sako* also allegedly teaches how to control the release of drug in a specific amount of time and that, if a release time of more than 12 hours is desired, that a polymer having a higher molecular weight should be used. (*Id.*) Based on these alleged teachings, the Examiner concludes that it would have been obvious to combine

Sako's disclosure of PEO to the combination of *Brann*, *Suzuki*, and *Shin* to produce a sustained release formulation comprising (-) - (S) -2,8-dimethyl-3-methylene-1-oxa-8-azaspiro[4.5]decane and to adjust the molecular weight according to the amount of release needed to prolong the action of the compound on lacrimal and salivary glands. (*Id.*) According to the Examiner, the skilled artisan would be motivated to make this combination because *Sako* allegedly teaches PEO as a preferred polymer to obtain these results. (*Id.* at page 7.) Applicant respectfully traverses with regard to claims 1-4 and 8-10, which are pending.

First, the combination of *Brann*, *Suzuki*, *Shin*, and *Sako*, at best may make it obvious to try using (-) - (S) -2,8-dimethyl-3-methylene-1-oxa-8-azaspiro[4.5]decane in the sustained release formulations taught in *Sako*. However, as MPEP § 2143 instructs, obvious to try can form the foundation for an obviousness rejection only under limited circumstances in which the Examiner must demonstrate 4 elements: (1) a finding that at the time of the invention there was a recognized problem or need in the art; (2) a finding that there had been a finite number of identified, predictable solutions to the recognized need; (3) a finding that one of ordinary skill in the art could have pursued these solutions with a reasonable expectation of success; and (4) additional factual findings to support the conclusion of obviousness. Regarding element (2), *Sako* presents the skilled artisan with an infinite number of possible drugs that might be used with its sustained release formulations, not a "number of finite, predictable solutions" as required by the MPEP.

Moreover, even if one were to suggest that the number of drug possibilities was finite and testable by the skilled artisan, the outcome of testing each drug is far from

predictable. Each of these drugs may have chemical properties that make them difficult to use with the compositions of *Sako*. For example, *Sako* teaches that various forms of drugs may need to be solubilized before use, "according to the particular drug." See col. 3, lines 21-45. Indeed, each of the drug categories listed in Sako encompasses drugs with very different chemical structures each of which can interact with the components of a sustained release formulation differently. Indeed, Applicants note that (-) - (S) -2,8-dimethyl-3-methylene-1-oxa-8-azaspiro[4.5]decane is not included in any of the drug categories listed in *Sako* at column 2, line 32 to column 3, line 20. Thus, Sako does not teach that (-) - (S) -2,8-dimethyl-3-methylene-1-oxa-8-azaspiro[4.5]decane could be used in a sustained release composition.

Finally, like *Brann*, neither *Suzuki*, *Shin*, nor *Sako* teach "a sustained release composition . . . wherein the release rate of the active ingredient from the composition is from about 4 percent per hour to about 50 percent per hour, wherein the maximum concentration of the active ingredient in plasma is about 150 ng/ml or less, and wherein the ratio of the maximum concentration to the minimum concentration of the active ingredient in plasma is about 91 or less." The combination of these references fails to teach this element of independent claim 1. For this reason and the reasons set forth above, claims 1-4 and 8-10 cannot be obvious in light of the combined teachings of *Brann*, neither *Suzuki*, *Shin*, nor *Sako*. Applicant requests that the Examiner withdraw this rejection.

Conclusions

Applicant respectfully requests that this Amendment under 37 C.F.R. § 1.116 be entered by the Examiner, placing claims 1-4 and 8-13 in condition for allowance.

Applicant submits that the proposed amendment of claim 1 does not raise new issues or necessitate the undertaking of any additional search of the art by the Examiner, since all of the elements and their relationships claimed were either earlier claimed or inherent in the claims as examined. Therefore, this Amendment should allow for immediate action by the Examiner.

Moreover, the entry of the Amendment would place the application in better form for appeal, should the Examiner dispute the patentability of the pending claims.

In view of the foregoing remarks, Applicant submits that this claimed invention is neither anticipated nor rendered obvious in view of the prior art references cited against this application. Applicant therefore requests the entry of this Amendment, the Examiner's reconsideration and reexamination of the application, and the timely allowance of the pending claims.

Please grant any extensions of time required to enter this response and charge any additional required fees to Deposit Account No. 06-0916.

Respectfully submitted,

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